UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: February 8, 2010

SUBJECT: Tolerance Exemption Petition Review in Support of Acetic Acid.

Decision Number: 389083 and 390013
DP Number: 366445 and 367757
EPA Petition Number: 8F7319
Chemical Class: Biochemical
PC Code: 044001
CAS Number: 64-19-7
Active Ingredient Tolerance Exemptions: 40 CFR 180.1258
MRID Numbers: N/A

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~~**THE FOLLOWING CONTAINS CONFIDENTIAL BUSINESS INFORMATION**~~

ACTION REQUESTED

On behalf of SummerSet Products, SciReg, Inc. has submitted a tolerance exemption petition for the active ingredient, acetic acid. The two products that are pending registration (EPA File Symbol Numbers 84069-R and 84069-E) contain acetic acid as an active ingredient and are intended for use in commercial and residential applications as non-selective contact herbicides on broadleaf plants and grass.

RECOMMENDATIONS AND CONCLUSIONS

Executive Summary

The available information and data are sufficient to support the request for an exemption from the requirement of a tolerance for acetic acid in or on all raw or processed agricultural commodities. The Agency has considered acetic acid in light of the relevant safety factors in FQPA and FIFRA. A determination has been made that no unreasonable adverse effects to the U.S. population in general, and to infants and children in particular, will result from the use of acetic acid when label instructions are followed. This conclusion is primarily based upon the following: 1) the unlikelihood of significant residues because exposure to desirable plants would be accidental or due to drift and would have deleterious effects to nontarget plants; 2) the concentration of acetic acid applied to target plants is comparable to that found in vinegar, which is commonly consumed by humans and application will likely result in residues that are substantially lower than general dietary exposures; 3) acetic acid rapidly biodegrades in the environment; 4) the chemical is practically non-toxic at pesticidal use concentrations (with the exception of severe eye irritation) and is readily metabolized in the body; and 5) humans are already generally exposed to the active ingredient, as it is ubiquitous in food and in the environment. Pesticidal uses of acetic acid are not expected to contribute significantly to the overall exposure of the general population to acetic acid.

STUDY SUMMARIES

Chemical Identity and Uses of Acetic Acid

Two end-use products are pending registration which contain acetic acid as an active ingredient. These products are intended for use as contact herbicides on broadleaf weeds and grass. These products are not intended to be directly applied to desirable plants (e.g.: food crops).

Acetic acid is a naturally-occurring substance found in all plants and animals. It is a component of aerobic metabolism, where it enters the Citric Acid Cycle combined with Coenzyme A, as Acetyl Coenzyme A. Additionally, acetic acid is readily metabolized by the tissues of the body and is used in other biochemical pathways, including the synthesis of proteins and intermediates of carbohydrates and fatty acids (JECFA, 1967).

The chemical is found in vinegar, a commonly consumed food, in concentrations ranging from 3-8%. Vinegar is also a commonly used household cleaner. Acetic acid can be produced synthetically and biologically, and is generally produced biologically by bacteria from the genus *Acetobacter* for use in vinegar. It may be used as a food additive in a multitude of foods including processed fruit, vegetables, dairy products, breakfast cereals, processed meats, condiments, beer and wines (CODEX GSFA, 2009). The chemical is also found naturally in a variety of foods, including coffee, edible plants, wines, seafood, meats and brown sugars. Acetic acid is an ingredient in medications and is also used as an antimicrobial. It is also used in the production of various chemicals, lacquers and explosives. The primary routes of exposure to the

general population have been determined to be through consumption of food and inhalation of air in workplaces. (HSDB, 2010) Acetic acid is considered to be Generally Recognized as Safe (GRAS) by the Food and Drug Administration (FDA) under 21 CFR 184.1005 as a direct food substance and under 21 CFR 582.1005 as a general purpose food additive.

An exemption from the requirement of a tolerance is established in 40 CFR 180.1258 for residues acetic acid when used as an active ingredient as a preservative on post-harvest agricultural commodities intended for animal feed, including Alfalfa, seed; alfalfa, hay; barley, grain; bermudagrass, hay; bluegrass, hay; bromegrass, hay; clover, hay; corn, field, grain; corn, pop, grain; cowpea, hay; fescue, hay; lespedeza, hay; lupin; oat, grain; orchardgrass, hay; peanut, hay; timothy, hay; vetch, hay; and wheat, grain, or commodities described as grain or hay. The active ingredient is also approved for use on growing crops or raw agricultural commodities after harvest as an inert ingredient in pesticide products under 40 CFR 180.910.

Toxicological Profile of Acetic Acid and Hazard Assessment

The data presented in Table 1 below are a summary of the toxicity data and information pertaining to acetic acid.

Table 1.

Study Type/OPPTS Guideline	**LD_{50}/LC_{50}/Results**	**Toxicity Category**	**MRID**
Acute Oral Toxicity/OPPTS 870.1100	3,310 mg/kg (rats)[1] 4,960 mg/kg (mice)	III	JECFA, 1967
Acute Dermal Toxicity/OPPTS 870.1200	1,060 mg/kg[1]	II	47330503
Acute Inhalation Toxicity/OPPTS 870.1300	> 11.4 mg/L[2] 5620 ppm (1hr)	IV	47330503
Acute Eye Irritation/OPPTS 870.2400	Corrosive	I	47330503
Acute Dermal Irritation/OPPTS 870.2500	Corrosive[3]	I	47330503
Skin Sensitization/OPPTS 870.2600	Inconclusive. Skin sensitization is rare, but has occurred. Data on pending EPs are negative for skin sensitization	N/A	47330504
Mutagenicity/OPPTS 870.5100 and 870.5300	Not mutagenic (Ames and CHO Assay)	N/A	47330503

90-Day Feeding/OPPTS 870.3100	LOAEL = 390 mg/kg bw-day (based on weight loss likely due to anorexia) NOAEL = 195 mg/kg bw- day	N/A	R.S. Jones to D. Benmhend, 2004
90-Day Dermal /OPPTS 870.3100	Waived due to limited exposure; repeat prolonged exposure not expected based on EP use pattern, PPE and REI	N/A	N/A
90-Day Inhalation/OPPTS 870.3100	Waived due to limited exposure; unlikelihood of significant levels of repeated inhalation exposure. Proposed EPs are liquids.	N/A	47330503
Developmental Toxicity/OPPTS 870.3700	LOAEL > 1,600 mg/kg bw-day NOAEL = 1,600 mg/kg bw-day	N/A	47330503

[1]Results using glacial acetic acid (>99% purity) as test substance
[2]Results using 96% acetic acid as test substance
[3]Results using 60% acetic acid as test substance

90-day Feeding

Weight loss was observed in rats administered up to 390 mg/kg bw-day acetic acid in drinking water for 2-4 months. The reduction in weight gain is likely attributed to reduced appetite and food consumption observed in the study. No other effects were reported. The lowest adverse effect level (LOAEL) was determined to be 390 mg/kg bw-day, and the no-observed adverse effect level (NOAEL) was determined to be 195 mg/kg bw-day.

90-Day Dermal and 90-Day Inhalation

These studies have been waived at this time. Given the use pattern and personal protection equipment (PPE) requirements of the products containing the active ingredient, repeated dermal and inhalation exposure is not expected to occur.

With regard to dermal exposure, the use does not involve purposeful application to the skin, nor will it result in prolonged dermal exposure to the product when label directions are followed. Acute toxicity testing of the two proposed end-use products in which acetic acid will be used as an herbicide have indicated that the products are non-irritating to slightly-irritating to the skin. Applicators are required to wear protective eye-wear, long-sleeved shirts, long pants, socks and shoes. Additionally, a restricted-entry interval (REI) of 48 hours has been added to these labels.

With regard to inhalation exposure, uses are unlikely to result in significant levels of repeated inhalation exposure, as the proposed EPs are liquids. Additionally, the concentration of the acetic acid in the proposed EPs is relatively low (approximately 8%). Based on the results of toxicity testing, the proposed EPs are placed into Toxicity Category IV for acute inhalation toxicity. To further mitigate exposure, a restricted-entry interval (REI) of 48 hours has been added to these labels.

Prenatal Developmental

Presumed pregnant adult female albino CD-1 mice were intubated orally with acetic acid beginning on day 6 of gestation at concentrations of 0, 16, 74, 345, and 1600 mg/kg bw-day. The animals were observed daily and body weights were recorded for 10 days. Caesarian sections were performed on day 17 on all dams. At this time, the numbers of implantation sites, resorption sites, and live and dead fetuses were recorded and general external and internal examinations were also made. There were no observed effects on nidation or on maternal or fetal survival at doses up to 1600 mg/kg bw/day. Abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the controls. The LOAEL is > 1600 mg/kg bw-day and the NOAEL is = 1600 mg/kg bw-day.

Similar studies were conducted on Wistar rats and Dutch rabbits using the same doses in the mouse study discussed above. Results of both studies were identical to the mouse study in that there were no observed effects on nidation or on maternal or fetal survival at doses up to 1600 mg/kg bw/day and abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the controls.

Mutagenicity

Results were negative for mutagenicity in bacterial reverse mutation assays (Ames test) where five strains of *Salmonella typhimurium* (TA 98, TA 100, TA 1535, TA 1537 and TA 1538) were exposed to concentrations of acetic acid from 0 to 10,000 µg/plate with and without metabolic activation.

In an *in vitro* Chinese hamster ovary (CHO) assay, results were also negative for mutagenicity. Acetic acid was not clastogenic at concentrations ≤ 16 mM, which was close to cytotoxic concentrations.

Effects on the Endocrine System

EPA is required under section 408(p) of the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally-occurring estrogen, or other such endocrine effects as the Administrator may designate." Acetic acid is not a known endocrine disruptor nor is it related to any class of known endocrine disruptors.

Exposure

Dietary Exposure-Food

Refer to the Chemical Identity and Uses of Acetic Acid section above for information regarding current uses and occurrence of acetic acid.

Products containing acetic acid for herbicidal use are not directly sprayed onto desirable plants. Accidental drift would result in deleterious effects to nontarget plants. Only accidental application or drift are anticipated. Application rates are low. At a hypothetical application rate of 1 gallon/1000 ft^2, the expected quantity of product per square inch of plant surface would be 0.026 ml of product, or 0.0021 ml acetic acid. Additionally, exposure is further mitigated in that both proposed end-use products may not be reapplied more than once every two weeks, per label instructions. The concentration of acetic acid applied to target plants (approximately 8%) is comparable to that found in vinegar, which is commonly consumed by humans. Accidental application or drift would likely result in substantially lower residues than those in the general diet. Should accidental application or drift occur, it is unlikely that residues of toxicological concern would be present.

Acetic acid biodegrades readily under both anaerobic and aerobic conditions. In one study using garden soil as inoculum, a 75% degradation was observed in 14 days. The results of a second study indicated a half-life of 24 minutes for radio-labeled acetic acid in soil. The chemical may also volatilize from dry surfaces based on its vapor pressure (approximately 15.7 mm Hg at 25° C). (HSDB, 2010) Because acetic acid biodegrades rapidly in the environment, residues of toxicological concern are not expected.

Dietary exposure is not expected at a level of toxicological concern due to the following: 1) the unlikelihood of significant residues because exposure to desirable plants would be accidental or due to drift and would have deleterious effects to nontarget plants; 2) the concentration of acetic acid applied to target plants is comparable to that found in vinegar, which is commonly consumed by humans and application will likely result in residues that are substantially lower than general dietary exposures; 3) acetic acid biodegrades in the environment rapidly; 4) the chemical is practically non-toxic at pesticidal use concentrations (with the exception of severe eye irritation) and is readily metabolized in the body; and 5) humans are already generally exposed to the active ingredient, as it is ubiquitous in food and the environment. Pesticidal uses are not expected to contribute significantly to the overall exposure of the general population to acetic acid.

Dietary Exposure-Drinking Water

Exposure of humans to acetic acid from pesticidal use in drinking water is unlikely. Products are not applied directly to water. Potential exposure to surface water would be negligible. Additionally, low application rates and rapid biodegradation contribute to the reduction in the

potential for exposure. Drinking water exposure is not expected to pose any quantifiable risk due to a lack of residues of toxicological concern.

Non-Dietary Exposure-Dermal and Inhalation Exposure

The potential for non-dietary exposure of the general population, including infants and children, is limited based on use patterns, PPE and REI requirements on product labels, and lack of anticipated residues of toxicological concern. Non-dietary exposures would not be expected to pose any quantifiable risk to the general population.

Occupational Exposure and Risk Assessment

Appropriate precautionary language has been provided on the proposed product labels. PPE requirements are protective eyewear, long-sleeved shirt, long pants and shoes and socks. An REI of 48 hours has also been added to the labels. Significant exposure is not expected due to PPE and REI requirements. There is reasonable certainty of no harm to residential and commercial workers and applicators based on PPE and REI requirements, low application rates, low toxicity of acetic acid, and rapid biodegradation of the chemical in the environment.

Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly Infants and Children

FFDCA section 408 provides that EPA shall apply an additional tenfold margin of exposure (safety) for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database, unless EPA determines that a different margin of exposure will be protective for infants and children. Margins of exposure are often referred to as uncertainty or safety factors. For the proposed pesticidal uses, based on all the available information, the Agency concludes that acetic acid is practically non-toxic (with the exception of severe eye irritation) to mammals, including infants and children. Thus, there are no threshold effects of concern and as a result, the provision requiring an additional margin of safety does not apply. Further, the provisions of consumption patterns, special susceptibility, and cumulative effects do not apply. Acetic acid is found in many foods already consumed by infants and children and there is no information available indicating an appreciable difference in risk between adults and infants and children from exposure to acetic acid when used as a contact herbicide. As a result, EPA has not used a margin of exposure approach to assess the safety of acetic acid. When used as proposed, it is not expected that the contact herbicides containing acetic acid as an active ingredient would result in residue levels that are of toxicological concern.

Aggregate Exposure

There is reasonable certainty that no harm to the US population will result from aggregate exposure to residues of acetic acid. This includes all exposures for which there is reliable information. The Agency arrived at this conclusion based on the low level of toxicity of the chemical (with the exception of severe eye irritation), low anticipated dietary and non-dietary exposures, worker protection requirements on the label (PPE and REI requirements) and the

already widespread exposure without any reported adverse effects on human health. The risks from aggregate exposure via oral, dermal and inhalation exposure are negligible. Aggregate exposures from pesticidal uses of acetic acid are not of concern to the Agency.

Cumulative Effects

Except for ocular exposure, pesticidal use of acetic acid is considered to be practically non-toxic. Cumulative effects with other substances with common mechanisms of toxicity are negligible.

Risk Characterization

The Agency has considered acetic acid in light of the relevant safety factors in FQPA and FIFRA. A determination has been made that no unreasonable adverse effects to the U. S. population in general, and to infants and children in particular, will result from the use of acetic acid when label instructions are followed.

REFERENCES

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cc: A. L. Gonzales, C. Greene, BPPD Science Review File, IHAD/ARS
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